
Human Health Ambient Water Quality Criteria (AWQC)

Water Quality Standards Academy

11-23-11

1

Slide 1

Background

- A Human Health AWQC is the highest concentration of a pollutant in water that is not expected to pose a significant risk to human health.
- EPA publishes two types of human health criteria:
 - Protection from ingesting water and aquatic organisms
 - Protection from ingesting aquatic organisms only

11-23-11

2

Slide 2

The human health criteria are estimates of concentrations of pollutants in ambient water that are not likely to pose a significant risk to the exposed human population. (*Ambient refers to open waters such as rivers, lakes and streams, as opposed to closed water supply systems that distribute treated water or wastewater*) This module will introduce the basic concepts that are used in the development of human health criteria and methods for deriving criteria.

Section 304(a)(1) of the Clean Water Act requires EPA periodically to review and publish criteria for water quality that accurately reflect the latest scientific knowledge on the kind and extent of all identifiable effects on human health and welfare.

These criteria are not Federal regulations; however, they are sometimes used by the States and authorized Indian Tribes to establish standards. They present scientific data and guidance on the effects of pollutants that can be used to derive regulatory requirements, including the promulgation of water quality-based effluent standards (*the Clean Water Act, section 302*), water quality standards (*the Clean Water Act, section 303*), or toxic pollutant effluent standards (*the Clean Water Act, section 307*).

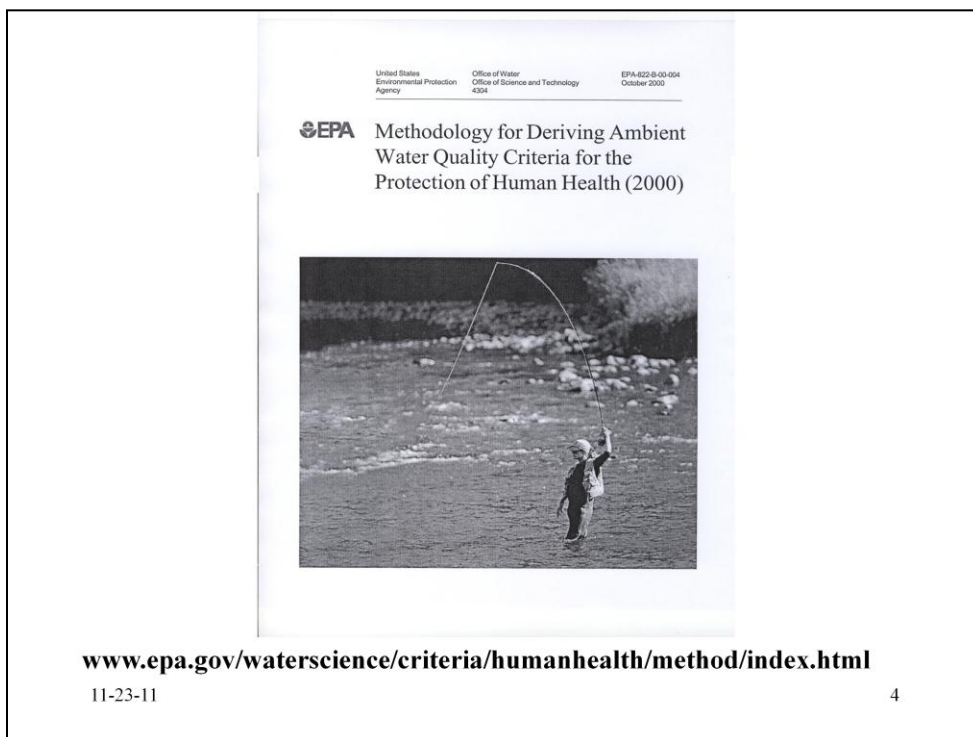
Equations for Deriving AWQC

- Noncancer Effects:
$$AWQC = RfD \cdot RSC \cdot \left(\frac{BW}{DI + \sum_{i=2}^4 (FI_i \cdot BAF_i)} \right)$$
- Cancer Effects:
 - Nonlinear
$$AWQC = \frac{POD}{UF} \cdot RSC \cdot \left(\frac{BW}{DI + \sum_{i=2}^4 (FI_i \cdot BAF_i)} \right)$$
 - Linear
$$AWQC = RSD \cdot \left(\frac{BW}{DI + \sum_{i=2}^4 (FI_i \cdot BAF_i)} \right)$$

11-23-11

Slide 3

This slide presents the three equations used to calculate human health (HH) Ambient Water Quality Criteria (AWQC). The equation selected will differ depending on the chemical contaminant and the type of adverse health effect associated with that chemical. This lecture focuses on the appropriate use for each equation and the data elements required in solving the selected equation. We will return to these equations several times during this presentation.



Slide 4

In 2000, EPA updated its guidance for deriving human health water quality criteria. Today's presentation is based on the 2000 Human Health Methodology. The methodology Document is available at <http://www.epa.gov/waterscience/criteria/humanhealth/method/method.html>

In addition to the Methodology document, there are two technical support documents that accompany the methodology. One covers the toxicology components of the methodology and the other the bioaccumulation components. Two additional technical support documents on exposure assessment and development of site-specific bioaccumulation factors are presently being developed and will be added to the web site when they are completed.

<http://www.epa.gov/waterscience/criteria/humanhealth/method/supportdoc.pdf>

<http://www.epa.gov/waterscience/criteria/humanhealth/method/tsdvol2.pdf>

The most recent human health criteria developed by EPA have been published in its Compilation of National Recommended Water Quality Criteria in 2006.

<http://www.epa.gov/waterscience/criteria/nrwqe-2006.pdf>

The criteria are similarly presented in tabular form on EPA's website at the following address:

<http://www.epa.gov/waterscience/criteria/wqcriteria.html>

Data Needs

- Toxicity
 - Toxic effects and dose-response properties
 - Risk Specific Doses for linear carcinogens
 - Point of Departure (POD)/Uncertainty Factor (UF) for nonlinear carcinogens
 - Reference dose (RfD) for noncarcinogens
- Exposure
 - Relative Source Contribution (RSC)
 - Exposure parameters: body weight (BW) drinking water intake (DI) and Fish Intake (FI)

11-23-11

5

Slide 5/6

The data requirements for development of the Human Health Criteria parallel the three topic areas of the 2000 Human Health Methodology:

Toxicology

Exposure

Bioaccumulation

These disciplines provide the data input parameters required for calculation of the human health AWQC criteria. The objective of this lecture is to familiarize you with the three equations, their data requirements, and the situations that lead you to choose one equation over the other.

The first term in each of the AWQC equations (Slide 3) is the Toxicology term. Toxicology provides information on the nature of the adverse effects that can be caused by the pollutant under consideration and the doses that cause the effect. Effects can range from mild dermatitis to birth defects or cancer. In toxicology, noncancer effects are generally considered separately from cancer effects. The specific dose-response terms that are used in the derivation of the human health criteria are as follows.

- Risk specific dose: The concentration in water that has a specific associated risk such as a one-in-a-million extra risk for an adverse effect. This dose-response parameter is used for chemicals that have no safe dose and where the risk increases linearly as dose increases from no exposure to doses where the tumors have been experimentally observed in one or more toxicological studies.
- The Point of Departure (POD) is the lower confidence bound on the lowest experimental dose that showed an effect. The critical study used for all quantitative risk assessments has a point of departure. However, at present, the POD acronym is primarily used in deriving the AWQC for a type of cancer that does not show a linear response to dose.
- The Reference Dose Terminology is used for noncarcinogens. It is defined as an estimate (with uncertainty spanning perhaps an order of magnitude) of a daily oral exposure to humans (including sensitive subgroups) that is likely to be without an appreciable risk of adverse effects over a lifetime.

We will be coming back to each of these terms as we proceed with this lesson. They are very important and going over them more than once is beneficial.

Data Needs (contd.)

- Bioaccumulation factors (BAFs)
 - Site-specific BAFs or National BAFs
 - Use of site-specific BAFs encouraged
 - Trophic level data on accumulation of chemical in fish or shellfish

11-23-11

6

The AWQC Equations also include several terms that apply to the human exposure to the toxicant in water.

The Relative Source Contribution (RSC) defines the portion of the total exposure that comes from ingestion of water and fish from the ambient water body of interest. Other exposure information such as that from dietary, inhalation and dermal routes should be considered and accounted for as part of the Relative Source Contribution human exposure analysis.

Other important exposure parameters are the body weight for the human receptors of interest and their intakes of drinking water and fish from the water body of interest. We will examine these exposure factors in greater detail later in this lesson

The last data set that is needed to solve the Human Health AWQC equations applies to bioaccumulation of the toxicant of interest in the fish and shellfish from the water body of interest. Bioaccumulation reflects the tendency for the concentration of the toxicant to increase as it moves from the water column through the aquatic food web to the species of interest. National default bioaccumulation factors are available in the Technical Support Document. The bioaccumulation factors can also be selected to match the specific species of interest based on its position (trophic level) in the food web or for intake of fish from a combination of different trophic levels. A third option (the preferred option) is collecting data in the field from which to derive a site specific bioaccumulation factor. Details on bioaccumulation will also be covered later in the lecture.

Types Of Effects: Historical View

- **Cancer effects**
 - Nonthreshold
 - Some risk at all doses
 - Linear response to dose
- **Noncancer effects**
 - Threshold
 - Acute, subchronic, or chronic
- **Organoleptic effects**
 - Taste, Odor, Color, etc.

11-23-11

7

Slide 7

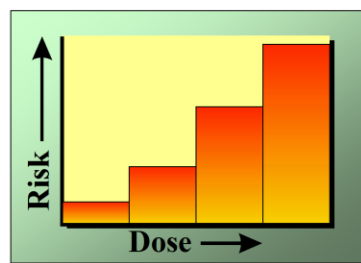
Health effects for toxic substances have historically been divided into two categories based on the biological endpoints observed:

- Carcinogenic effects which have some effects at all doses (lack a threshold) and demonstrate a linear response to dose
- Noncancer effects which have a threshold and exhibit acute, subacute, or chronic toxicity

In a few cases, taste and odor (organoleptic) data form the basis for nonregulatory HH criteria. These criteria are established when there is insufficient information on toxicological effects and the chemical has an objectionable impact on the taste or odor of the water, or when the pollutant level estimate based on taste and odor effects is lower than the level calculated from the toxicological data. A criterion derived from organoleptic data does not necessarily represent a value that adversely affects human health. It is presented as an estimate of the level of a pollutant that will not produce unpleasant tastes or odors for person consuming water or aquatic organisms found in ambient waters.

Nonthreshold Effects

- All Levels of exposure pose some probability of an adverse response
- Incremental risk levels can be calculated
- EPA targets a risk level of one in one million (10^{-6})



11-23-11

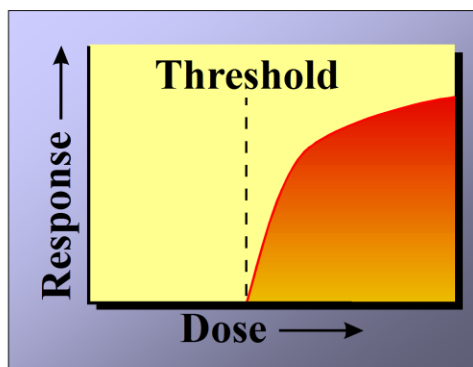
Slide 8

Traditionally all cancer effects were considered to lack a threshold. This means that there is some risk for all levels of exposure between a dose of zero and the lowest observed tumor response, and that the risk increases in a linear fashion defined by the slope of the line. The slope of the line is termed the cancer slope factor (CSF) or Q1*. It is used to derive the Risk Specific Dose found in the equation for linear carcinogens. The linear approach is used for direct-acting carcinogenic agents, those that cause chemical changes (mutations) in DNA. It is also the default choice for carcinogens when there are insufficient data to demonstrate that the mode of action of the chemical is nonlinear (Human Health AWQC Equation 1).

EPA's criteria for evaluating linear carcinogens targets an incremental increased risk of cancer at a level of one in one million, or at a 10^{-6} level. EPA also provides an acceptable risk range for states and authorized tribes between 10^{-6} and 10^{-4} risk level. However, states and authorized tribes must ensure that the risk to more highly exposed subgroups does not exceed the 10^{-4} level.

Threshold Effects

Exposures to some finite value are expected to be without adverse effect on human health

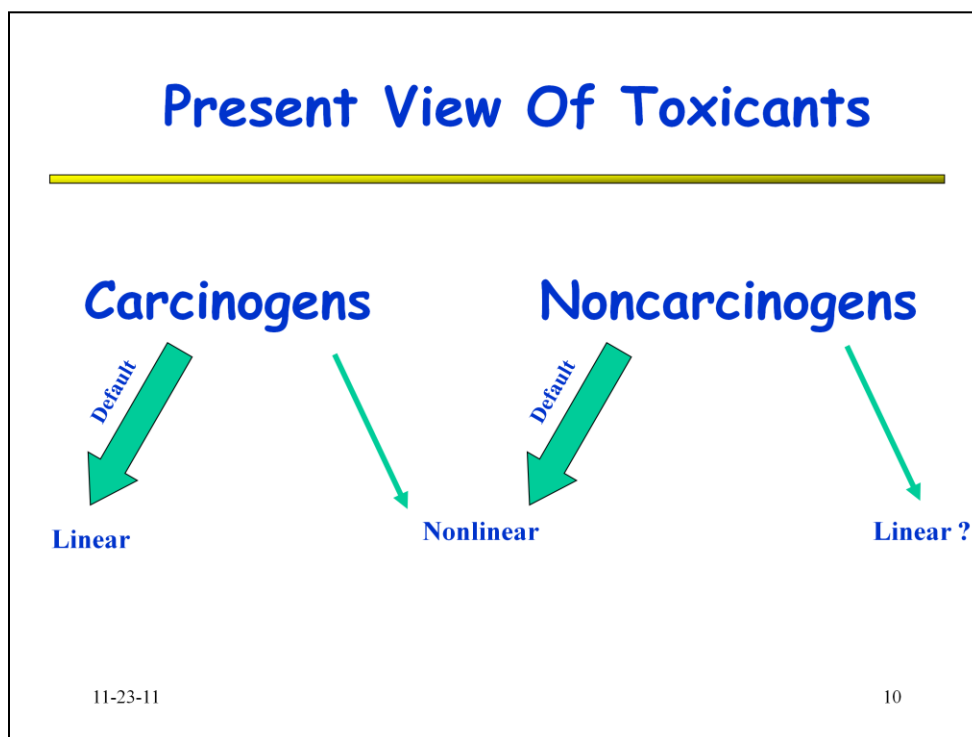


11-23-11

9

Slide 9

Threshold toxicants, on the other hand, have been treated as if there is an exposure threshold below which there are no effects. Threshold chemicals produce adverse effects other than cancer in humans and/or animals due to their effects on the function of various organ systems. These chemicals have been assumed to have safe exposure levels up to a certain threshold concentration. The threshold hypothesis holds that a range of exposures from zero to some finite value can be tolerated with essentially no effect on human health (Human Health AWQC Equation 3). Exceptions to this rule are the essential trace elements (such as zinc and selenium) where adverse effects are manifest at low doses because there is an insufficient intake of the nutrient to support its function. This situation is called deficiency rather than toxicity. The dose-response curve for nutrients has a u-type shape with adverse consequences for both low and high doses.



Slide 10

As greater insight has been obtained into the mechanism(s) of toxicity for a wide variety of toxicants, it is becoming more and more obvious that separating carcinogenic and noncarcinogenic chemicals into nonthreshold and threshold modes of action was a naive approach to risk assessment. Some carcinogens appear to act through an indirect threshold mechanism and do not show a linear response to dose as the dose approaches zero. Under the AWQC Methodology they are characterized by a nonlinear Point of Departure (POD) divided by uncertainty factors (Human Health AWQC Equation 2). We will discuss uncertainty factors used in this equation later in this lecture.

Linearity in the response to dose may also apply to some noncancer endpoints. Lead is the contaminant that is most frequently characterized in this way. Thus far, it has not been possible to define a dose for lead that has no effect.

Accordingly, we are seeing a shift from the traditional approach of viewing quantitative risk assessment for carcinogens as a linear process and noncancer assessments as nonlinear. Increasingly, the determination of whether to use a linear or a nonlinear approach is based on the mode of action for an effect more than whether the effect of interest is cancer or not.

In the next few slides we are going to examine the approaches used for the quantitative risk assessment for noncarcinogens and carcinogens (linear and nonlinear). We will examine the noncancer situation first. The processes we are about to discuss are used to generate the input toxicological parameters for Equation 1.

Noncancer Dose-response Values*

NONCANCER

- Reference Dose (RfD)
 - An estimate (with uncertainty spanning perhaps an order of magnitude) of a daily oral exposure to humans (including sensitive subgroups) that is likely to be without an appreciable risk of adverse effects during a lifetime.

* Risk values and complete toxicological assessments may be found on EPA's Integrated Risk Information System (IRIS) at www.epa.gov/iris

11-23-11

11

Slide 11

First we will look at the noncancer risk term in the Human Health AWQC equation. Remember, at present, all noncancer risk assessments assume that there are safe doses and that adverse effects from exposure exhibit a threshold.

As mentioned earlier, the noncancer toxicological parameter needed for calculation of an AWQC is the reference dose. The reference dose (RfD) is:

- An estimate (with uncertainty spanning perhaps an order of magnitude) of a daily oral exposure to humans (including sensitive subgroups) that is likely to be without an appreciable risk of adverse effects over a lifetime.

Reference dose information for individual chemicals can also be found on the EPA IRIS database (www.epa.gov/iris). Reference doses for pesticides are included in Re-registration eligibility Documents (REDs) that are available from the Office of Pesticide Programs (OPP) web site:

<http://www.epa.gov/pesticides/reregistration/status.html>

Noncancer Effects

- RfD Derivation
 - RfD = Point of Departure divided by Uncertainty Factor (UF)
- Point of Departure
 - No Observed Adverse Effect Level (NOAEL)
 - Lowest Observed Adverse Effect Level (LOAEL)
 - Benchmark Dose (BMD)

11-23-11

12

Slide 12

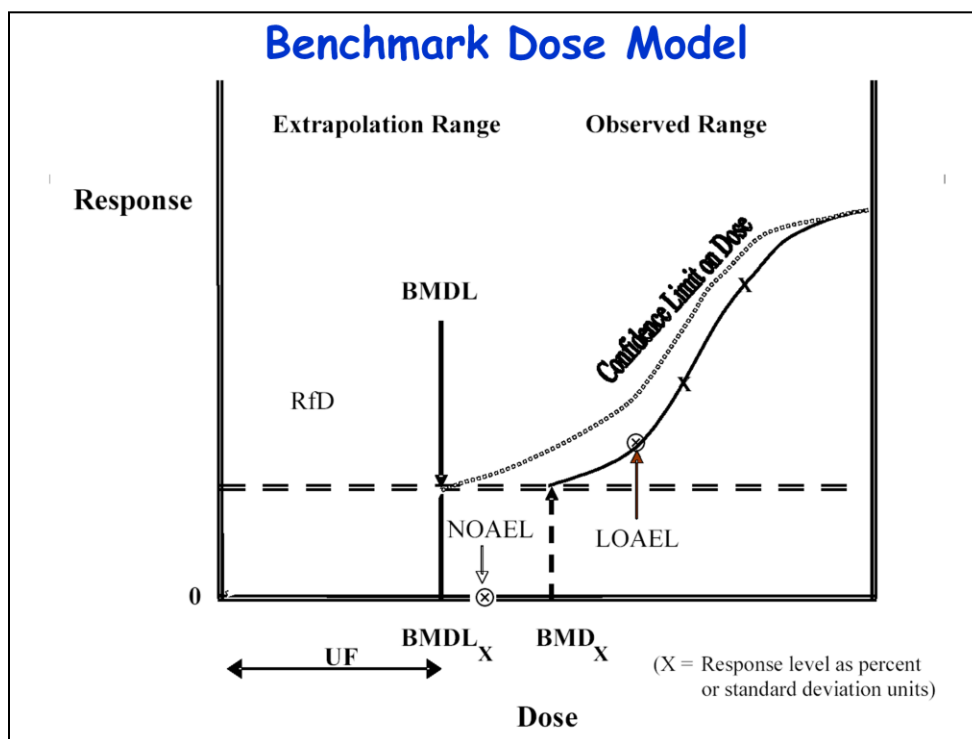
There are several points of departure that can be used in calculating a RfD. Most RfDs on IRIS were calculated using the NOAEL or LOAEL as the point of departure. These acronyms signify:

No Observed Adverse Effect Level (NOAEL) – The highest dose in a study or group of toxicological studies that has no associated adverse effect.

Lowest Observed Adverse Effect Level (LOAEL) – The lowest dose in a study or group of studies that shows an effect. The effect or effects observed at that dose is/are called the critical effect(s).

The study that identifies the NOAEL or LOAEL (the one used as the point of departure) is called the critical study.

Most recent EPA assessments for noncarcinogens use a Benchmark Dose assessment procedure to describe the experimental data. This approach has an advantage over the NOAEL/LOAEL approach in that it considers all of the dose-response data and models the dose response curve following a procedure very similar to that used for cancer.



Slide 13

This Figure illustrates the use of the Benchmark Dose approach to quantify an estimated safe dose for a noncancer effect. Depending on the exposed population, and the size and quality of the data set, the Benchmark Dose methodology can determine a Benchmark dose (BMD) for 10% (BMD_{10}), 5% (BMD_{05}) or 1% (BMD_{01}) of the study group. It can also model continuous data such as a change in average group body weight or the average serum levels of an enzyme that is a biomarker for cellular damage. The BMD in the case of continuous data is usually a 1 standard deviation or 0.5 standard deviation change from the control population.

The BMD modeling programs for noncarcinogens include several curve fitting options. Generally several models are applied and the one with the best fit to the dose-response is selected. A 95% confidence limit on the BMD is determined (BMDL) and that value is used as the point of departure for the RfD analysis. The RfD is derived by dividing the BMDL by a composite uncertainty factor.

Uncertainty Factors

- Five areas of consideration
 - Intraspecies variation (UF_H)
 - Interspecies variation (UF_A)
 - Uncertainty due to the duration of study (UF_S)
 - Uncertainty due to use of a LOAEL (UF_L)
 - Uncertainty due an inadequate database (UF_D)
- Invoked as integers of 1, 3, 10
 - 3 is a half \log_{10}
 - Value selected determined by the data available
 - Usually $\leq 3,000$

11-23-11

14

Slide 14

When evaluating the uncertainty factor that should be used in the determination of the RfD and for a carcinogen with a nonlinear response to doses, five areas of uncertainty are considered. They are:

UF_H - A factor of 1, 3 (approximately $\frac{1}{2} \log_{10}$ unit), or 10-fold factor used to account for variation in sensitivity among members of the human population (intraspecies variation).

UF_A - A factor of 1, 3 or 10 used to account for uncertainty when extrapolating from valid results of long-term studies on experimental animals to humans (interspecies variation).

UF_S - An factor of 1, 3 or 10 used to account for the uncertainty involved in extrapolating from less-than-chronic NOAELs to chronic NOAELs.

UF_L - A factor of 1, 3 or 10 used to account for the uncertainty involved in extrapolating from LOAELs to NOAELs.

UF_D - A factor of 1, 3 or 10 to account for the uncertainty associated with extrapolation from the critical study data on some of the key toxic endpoints lacking, making the database incomplete.

According to Agency policy, the individual uncertainty factors are applied in units of 1, 3 or 10 unless there are data that support the derivation of a more precise (data-derived) value. The 3 is a half log of 10. The individual uncertainty factors are multiplied together to determine the composite UF value used for both the RfD and POD/UF term for nonlinear carcinogens. When the precursor effect is the basis of the assessment for a nonlinear carcinogen rather than the tumors, the RfD can be described as protective for both cancer and noncancer effects and a separate nonlinear assessment is not necessary.

General Equation For Noncancer Effects

$$AWQC = RfD \times RSC \times \left[\frac{BW}{DI + (FI \times BAF)} \right]$$

AWQC = Ambient Water Quality Criterion (mg/L)

RfD = Reference Dose (mg/kg-day)

RSC = Relative Source Contribution (%; to account for other sources of exposure)

BW = Human Body Weight (kg, 70 for average adult)

DI = Drinking Water Intake (L/day, 2 for average adult)

FI = Fish Intake (kg/day)

BAF = Bioaccumulation Factor (L/kg)

11-23-11

15

Slide 15

The risk term in the noncancer equation is the RfD. A relative source contribution factor is used. Remember that this is a factor that looks at the portion of the total exposure that results from use of the ambient water body as a source of drinking water and/or fish/shellfish from that water body as a food.

The remaining terms in the equation are consistent across all three equations. Information about the exposure and BAF terms is presented after the toxicology segment of this lesson.

Carcinogen Dose-response Values*

- Risk Specific Dose (RSD) for linear carcinogens
 - RSD is the acceptable risk Level divided by the **Cancer Slope Factor**
 - EPA recommends 10^{-6} , (one in a million chance of cancer), but accepts the 10^{-5} risk level as long as highly exposed populations do not exceed 10^{-4} risk level
- POD/UF approach for nonlinear carcinogens

*** Risk values and complete toxicological assessments may be found on EPA's Integrated Risk Information System (IRIS) at www.epa.gov/iris**

11-23-11

16

Slide 16

We earlier identified the Risk Specific Dose (RSD) as the toxicology parameter that was used for Equation 3 and stated that the parameter is applied to those carcinogens that demonstrate a linear response to dose because of their ability to chemically change the structure of DNA.

The RDS is defined as: the dose in mg/kg/day that has a specific associated extra risk such as a one-in-a-million excess risk for an adverse effect.

EPA recommends using the RDS for a one-in-a-million excess risk (10^{-6} risk) but also accepts a one-in-a-hundred-thousand risk (10^{-5} risk) as long as the risk for highly exposed individuals does not exceed a one-in-ten-thousand (10^{-4}) risk. The term extra in the definition of the RDS refers to a risk from environmental exposure to the chemical of interest above the background risk that is always present.

The RSD is derived by dividing the risk of interest by the cancer slope factor (CSF or $q1^*$):

$$\text{RSD} = \frac{1/1,000,000}{\text{CSF}} = \frac{0.000001}{\text{CSF}^*}$$

The CSF or $q1^*$ values for individual chemicals can be located in their files on the EPA Integrated Risk Information system (IRIS) at www.epa.gov/iris.

A different approach is used for carcinogens that have a nonlinear response to dose or a threshold. In such an instance, a point of departure or an estimate of a dose near the bottom of the dose-response curve for tumors or a precursor effect is selected and divided by an uncertainty factor to arrive at the value that will be used to calculate the AWQC. The POD/UF approach is very similar to the RfD approach we have already discussed.

Cancer Descriptors

- Known human carcinogen
- Likely human carcinogen
 - Likely by all exposure routes
 - Likely at high doses but unlikely at low doses
 - Signifies a nonlinear mode of action
 - Likely by one route of exposure but for other exposure routes
- Suggestive evidence of carcinogenicity
 - In most cases dose response will not be quantified for chemicals with this descriptor
- Unable to make a determination about possible carcinogenicity
- Not a carcinogen

11-23-11

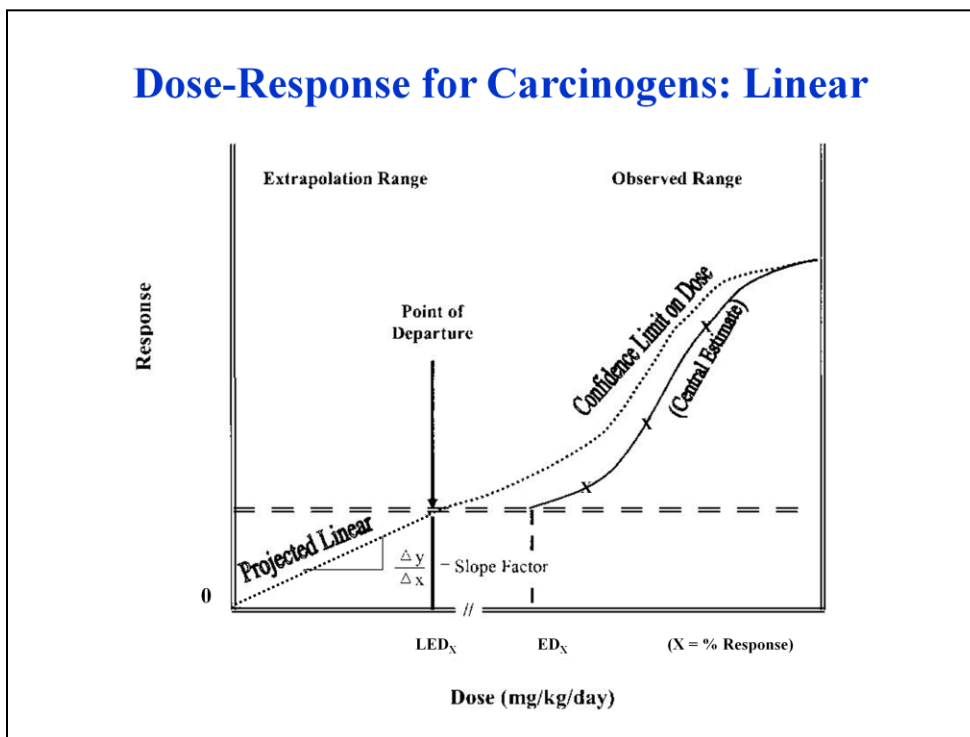
17

Slide 17

EPA characterizes chemicals on the basis of the weight-of-evidence regarding the ability to cause tumors and a slope factor which is a measure of the incidence of tumors relative to dose. At one time the Agency placed chemicals in groups based on weight of evidence. Group A chemicals were known human carcinogens. Group B chemicals were probable human carcinogens and group C chemicals were possible human carcinogens. A chemical was placed in group D if there were insufficient data to make a determination about its potential to cause cancer and Group D chemicals were those with adequate data that they did not cause tumors.

The Agency 2005 Guidelines for Carcinogen risk Assessment eliminated the cancer groupings and replaced them with descriptive terms. The transition to the new terminology began with the 1996 draft of what became the 2005 guidelines. The descriptive terms from the 2005 guidelines are listed on this slide. For those chemicals classified as being carcinogenic there are several options for the narrative statement. The classification can apply to all exposure routes or just one route. A chemical with a nonlinear mode of action can be described as likely high doses but unlikely as a lower dose that does not cause and identified precursor effect. It is this later group that utilizes the AWQC equation for a non-linear carcinogen.

Under the new classification scheme, it is expected that those chemicals that are characterized as having suggestive evidence of carcinogenicity will usually not be quantified for their cancer potency resulting in the use of the RfD approach to determining the HH guideline value



Slide 18

This figure is an illustration of the method that EPA uses to determine the cancer slope factor. The X axis in the Figure represents the doses of the carcinogen that were studied in the critical cancer study. The Y axis is the response observed in the experimental animals expressed in quantal terms (usually percent of animals with tumors). The Xs connected by a solid line in the graph represent the responses seen in the experimental animals at the doses administered in the critical study. Their location on the figure defines the dose range of observation.

The dotted line on the graph is generated by the multistage program from the EPA Benchmark Dose Software and represents the lower 95% confidence bound on the doses studied.

Usually EPA selects a 10% tumors response as the point of departure for the determination of the slope factor if that is justified by the data. Higher or lower response rates can also be selected as determined by the statistical power of the study. The statistical power of the study is a function of the number of animals in each dose group or the epidemiological power of the human data. The Effective Dose (ED) on the X axis denotes the effective lowest dose in the study and the x term the approximate percentage of that response; the LED is the lower bound on that dose. The LED is the point of departure for derivation of the slope factor. A straight line is drawn from the point of departure to the origin of the X/Y axes. The slope of the line is the change in the y axis divided by the corresponding change in the x axis. Its units are $(\text{mg/kg/day})^{-1}$.

General Equation For Linear Cancer Effects

$$AWQC = RSD \times \left[\frac{BW}{DI + (FI \times BAF)} \right]$$

AWQC = Ambient Water Quality Criterion (mg/L)

RSD = Risk Specific Dose (mg/kg-day)

BW = Human Body Weight (kg, 70 for average adult)

DI = Drinking Water Intake (L/day, 2 for average adult)

FI = Fish Intake (kg/day)

BAF = Bioaccumulation Factor (L/kg)

11-23-11

19

Slide 19

This slide shows the equation for linear carcinogens. You should now understand how the toxicology term in that equation is derived. Note that all remaining terms apply to exposure and bioaccumulation which will be discussed later in this lecture.

Remember the RSD is the risk you select (10^{-6} or 10^{-5} , as long as the exposed population risk is not greater than 10^{-4}) divided by the cancer slope factor. IRIS is the best source of cancer slope factor data for chemical contaminants.

Nonlinear Carcinogen

- Must know the mode of action (MOA) to use this approach
- Mode of Action must support a zero slope at a dose of zero
 - Only possible for nonmutagenic chemicals
 - A MOA is "a sequence of key events starting with interaction of an agent with a cell, proceeding through functional and anatomical changes, and resulting in cancer formation." (U.S.EPA, 2005)
- Select the POD for quantification
 - A POD based on an event in the mode of action that occurs before tumors is preferred
 - Examples
 - cytotoxicity,
 - regenerative hyperplasia (tissue repair)
 - Comparable to RfD derivation

11-23-11

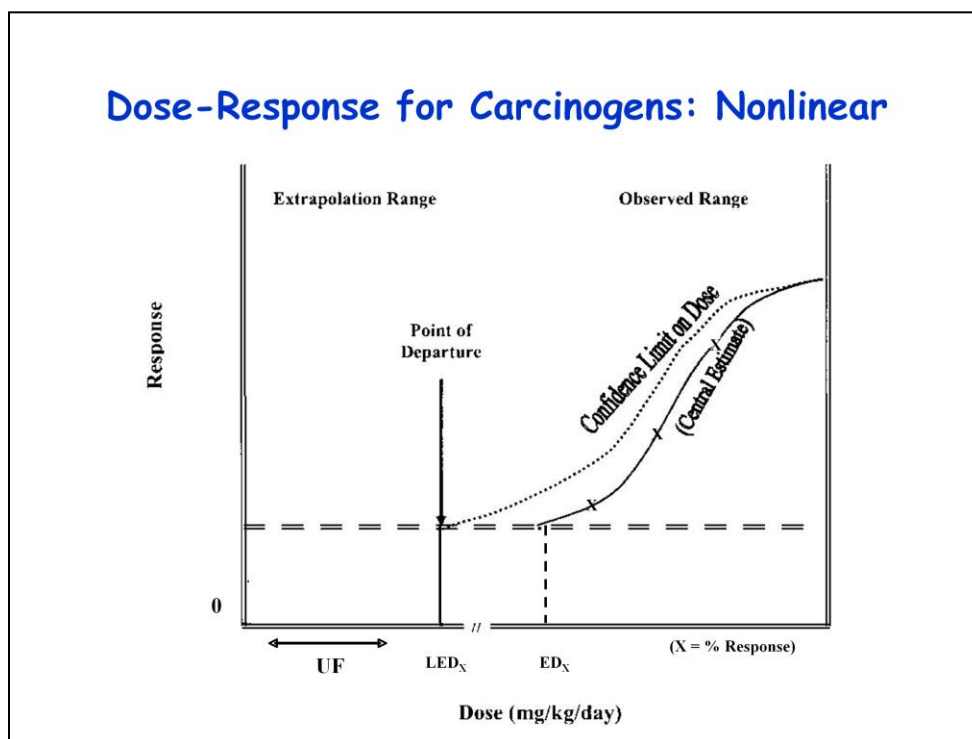
20

Slide 20

The nonlinear approach for derivation of the Human Health AWQC is only an option if the mode of action information is known and supports a zero slope at a dose of zero. In other words, there are some doses where there is no risk. This will not occur when the contaminant is mutagenic. When this is the case, Equation 2, which uses the POD/UF as the quantitative measure of risk, can be used in the calculation of the human health AWQC.

A mode of action is an experimentally documented sequence of key events starting with interaction of an agent with a cell proceeding through functional and anatomical changes and resulting in cancer formation. In other words, at doses below those that cause the precursor cellular events, there is no cancer risk.

A POD based on a precursor event in the MOA prior to tumor formation is preferred over tumor incidence. When based on a precursor event the derivation for the nonlinear carcinogen is comparable to the RfD derivation.



Slide 21

This Figure is very similar to that used for the carcinogens that have a linear response to dose except that there is no extrapolation of the dose response below the LED_x. The toxicological data plotted can be either tumor data or data (quantal or continuous) for a precursor event. Increasingly, the precursor data are increasingly being utilized for the cancer assessment. However, use of precursor data is usually analogous to establishing a RfD for a noncancer effect. As a general rule, the less one knows about the sequence of precursor events and the doses that cause them, the higher the uncertainty factor applied. Many times the types of studies that are used to document the mode of action are mechanistic studies that may not generate whole animal data on the doses that might cause a precursor event.

The 2000 AWQC Human Health Methodology discussed the use of a Margin of Exposure (MOE) approach to quantifying the acceptable nonlinear cancer risk number. The MOE was defined as the desirable difference between the point of departure and the environmental exposure. In some ways it was similar to a composite uncertainty factor. The final EPA Cancer guidelines (2005) discontinued the use of the MOE term. Instead of the MOE, the nonlinear assessments usually apply uncertainty factors to the LED_x.

General Equation For Nonlinear Cancer Effects

$$AWQC = POD/UF \times RSC \times \left[\frac{BW}{DI + (FI \times BAF)} \right]$$

AWQC = Ambient Water Quality Criterion (mg/L)

POD/UF = Point of Departure/Uncertainty Factor (mg/kg-day)

RSC = Relative Source Contribution (to account for other sources of exposure)

BW = Human Body Weight (kg, 70 for average adult)

DI = Drinking Water Intake (L/day, 2 for average adult)

FI = Fish Intake (kg/day) = Bioaccumulation Factor (L/kg)

BAF = Bioaccumulation factor (L/kg)

11-23-11

22

Slide 22

This slide shows the equation that is used for calculating the Human Health AWQC for a tumorigenic chemical with data to demonstrate that the tumors do not show a linear response to dose. The POD/UF value supplied the toxicological parameter for this equation.

It is important to remember that when mode of action information is absent or incomplete, the linear approach is used (Equation 3).

As was the case with Equation 1, the remaining terms in the equation are related to exposure and bioaccumulation. It is important to note that Equation 2 includes an exposure-related (RSC) term that is not in Equation 3.

Exposure Assessment

- There are two primary exposure sources of concern for deriving human health water quality criteria.
 - Direct ingestion of drinking water
 - Consumption of fish/shellfish
- Other sources of exposure to a given contaminant are also considered when deriving criteria for non-carcinogens and non-linear carcinogens, as part of the Relative Source Contribution (RSC) analysis.

11-23-11

23

Slide 23

The second groups of terms in the equations used to calculate the AWQC for human health apply to exposure. They focus on water and fish/shellfish from the water body being evaluated. The water ingestion exposure assumptions apply to both direct ingestion of water from the source, as well as ingestion of treated water from the source if the contaminant is unregulated. The inclusion of treated water covers situations where treatment may not remove the contaminant of concern. If the contaminant is unregulated, there is no way to know if it is being removed through treatment.

The fish/shellfish component of the exposure assessment pertains primarily to fish ingested by subsistence fishermen and sports fishermen but can also apply to fish caught locally and sold to the general population. Fish/shellfish consumption estimates vary with the population of interest.

The Relative Source Contribution (RSC) takes into account the portion of the total exposure that is contributed by the water plus fish/shellfish that originate from the ambient water body being evaluated.

Exposure Parameters and Protection Goals

- EPA generally assumes daily exposure over the course of a lifetime.
- EPA generally assigns a mix of average values and high end values (e.g., 90th percentile) for exposure parameters such as ingestion rates and body weight.
- EPA's criteria are derived to protect the majority of the general population.

11-23-11

24

Slide 24

In most cases the Human Health AWQC applies to the general adult population and assumes a lifetime exposure. However, there are some circumstances where pregnant women or children may be the population of interest. These would be situations where the critical effect on which the RfD is based applies to developmental effects that would impact the fetus during pregnancy or children during their period of physical maturation.

EPA's Default Exposure Parameters

$$AWQC = RfD \cdot RSC \cdot \left(\frac{BW}{DI + \sum_{i=2}^4 (FI_i \cdot BAF_i)} \right)$$

- BW = 70 kg; average adult body weight
- DI = 2 L/day; 90th percentile estimate
- FI = 17.5 g/day; 90th percentile estimate
- These parameters will be used by EPA for the national recommended water quality criteria when chronic health effects are of concern.

11-23-11

25

Slide 25

As stated on the previous slide, EPA uses a mix of average and 90% values in deriving the Human Health AWQC. There are the three exposure terms in the bracketed portion of the equation. They are the body weight, the drinking water intake and the fish/shellfish intake. The body weight is an average body weight while the drinking water and fish/shellfish intake values are 90% values.

The three exposure parameters given on this slide are those for adults. If children or pregnant women are the group of concern, alternate values will be used as detailed on the next slide.

The FI value (17.5 grams/day) is an estimate of the 90th percentile consumption of fish and shellfish from estuarine and fresh waters for adults in the general population. This value is also recommended as an estimate of average consumption of fish and shellfish from estuarine and fresh waters for recreational fishers.

Other Exposure Parameter Options

- In special circumstances, when the basis of a health assessment is a developmental effect, EPA recommends the following parameter values:
 - Women of childbearing age (ages 15-44), when fetal developmental effects are the most sensitive health endpoint
 - BW = 67 Kg; average body weight
 - DI = 2 L/day; 90th percentile estimate
 - Children
 - BW = 30 Kg; ages 1-14
 - = 13 Kg; toddlers (ages 1-3)
 - = 7 Kg; infants
 - DI = 1 L/day for all three sub-categories, above

11-23-11

26

Slide 26

As was the case for adults, the body weights used for women of childbearing age and children are averages for the population of concern while the drinking water intakes are 90 percentile values. Fish intake options for select populations are presented on the next slide.

Additional Fish Intake Values

- For chronic health effects when targeting:
 - Recreational fishers = 17.5 g/day
 - Estimate of 90th percentile consumption of freshwater/estuarine fish/shellfish;
 - Subsistence fishers = 142.4 g/day
 - High-end estimate of consumption of freshwater/estuarine fish/shellfish.
- For developmental health effects when targeting:
 - Women of childbearing age (re: fetal effects) = 165.5 g/day
 - Estimate of 90th percentile meal size of freshwater/estuarine fish/shellfish;
 - Children (ages 1-14) = 156.3 g/day
 - Estimate of 90th percentile meal size of freshwater/estuarine fish/shellfish.

11-23-11

27

Slide 27

In addition to the 17.5 g/day for its national recommended water quality criteria, EPA recommends the following intake for other groups of concern as appropriate.

17.5 grams/day is an estimate of the 90th percentile consumption of fish and shellfish from estuarine and fresh waters for adults in the general population. This value is also recommended as an estimate of average consumption of fish and shellfish from estuarine and fresh waters for recreational fishers;

• 142.4 grams/day is an estimate of average consumption of fish and shellfish from estuarine and fresh waters for subsistence fishers.

• 165.5 grams/day is an estimate of the 90th percentile consumption of fish and shellfish from estuarine and fresh waters for women of childbearing age (i.e., ages 15 to 44). This value represents the consumers-only data from the survey for this particular group; specifically, the survey respondents who actually consumed fish on any of the survey days (i.e., the non-zero values only). The point of considering consumers-only (as defined above) here is to produce an estimate of meal size for circumstances where acute or short-term exposures may result in adverse developmental health effects in the fetus.

• 156.3 grams/day is an estimate of the 90th percentile consumption of fish and shellfish from estuarine and fresh waters for children (i.e., ages 14 and under). This value represents consumers-only data (again, the non-zero consumption values only) from the survey for this particular group. The point of considering consumers-only here is to produce an estimate of meal size for circumstances where acute or sub-chronic exposures may result in adverse health effects in children.

All of the default intake values recommended are based on the uncooked weights of the fish analyzed. EPA strongly encourages States and authorized Tribes to use the results from local or regional fish intake surveys as more representative of their target population group(s).

Relative Source Contribution

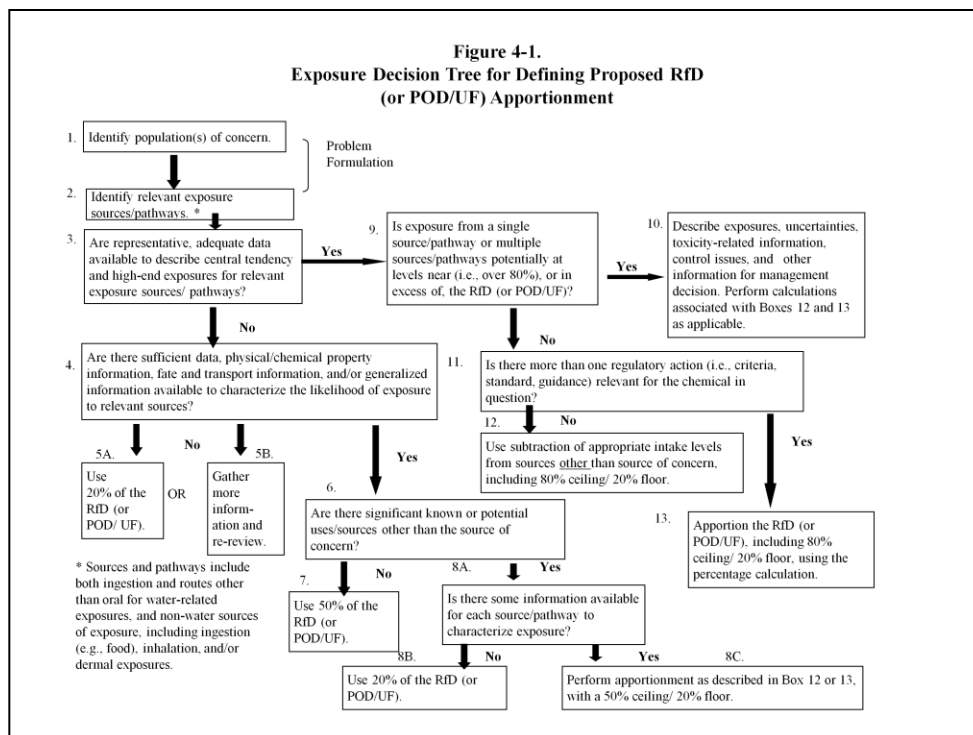
- Accounts for exposures from sources other than water and freshwater/estuarine fish and shellfish ingestion
 - Inhalation for airborne sources
 - Consumption of food
 - Consumption of marine aquatic organisms
- Not applied to linear carcinogens (i.e., those associated with a risk level)
- Expressed as a percentage of or subtracted from the RfD or nonlinear carcinogen depending on the circumstances

11-23-11

28

Slide 28

A complete human exposure evaluation encompasses not only estimates of exposure to the toxic pollutant of concern from ambient water fish/shellfish consumption, but also exposure by way of other exposure routes, including recreational contact, dietary intake (not including that from fish/shellfish from the water body of interest), inhalation of air, and consumption of marine aquatic organisms. An analysis of overall exposure based on available data and the contributions from each source is called the relative source contribution (RSC) analysis. A data-based RSC is determined when data are available. When data are not available, a default assumption is used. The HH Methodology provides a decisions tree approach to determining the RCS. The Decision Tree is shown on the next slide and the approach is described in Chapter 4 of the Methodology document.



Slide 29

A discussion of the decision tree is beyond the scope of this class. It is presented as an illustration of the fact that there are a number of steps and options available for the RSC. In the past most assessments used a 20% default assumption.

Independent of the process used in determining the RSC, there is a 20% floor and a 80% ceiling to account for the difficulty in identifying all possible routes of exposure.

Bioaccumulation

$$AWQC = \frac{POD}{UF} \cdot RSC \cdot \left(\frac{BW}{DI + \sum_{i=2}^4 (FI_i \cdot BAF_i)} \right)$$

11-23-11

30

Slide 30

In order to prevent harmful exposures to waterborne chemicals through the consumption of contaminated fish and shellfish, national 304(a) water quality criteria for the protection of human health address the process of chemical bioaccumulation in aquatic organisms.

When deriving national 304(a) criteria to protect human health, EPA accounts for potential bioaccumulation of chemicals in fish and shellfish through the use of national bioaccumulation factors (BAFs).

The goal of EPA's national BAF is to represent the long-term, average bioaccumulation potential of a chemical in edible tissues of aquatic organisms that are commonly consumed by humans throughout the United States.

A national BAF is a ratio (in L/kg) that relates the concentration of a chemical in water to its expected concentration in commonly consumed aquatic organisms **in a specified trophic level**.

Over the past two decades, much information has been assembled which demonstrates that an organism's trophic position in the aquatic food web can have an important effect on the magnitude of bioaccumulation of certain chemicals. In order to account for the variation in bioaccumulation that is due to trophic position of the organism, the 2000 Human Health Methodology recommends that BAFs be determined and applied on a trophic level-specific basis. Hence, three national BAFs are derived; one for aquatic organisms in each of trophic levels 2, 3, and 4. Accordingly the "FI times BAF" term in the equations is the sum of $(FI_{TL2} \times BAF_{TL2}) + (FI_{TL3} \times BAF_{TL3}) + (FI_{TL4} \times BAF_{TL4})$. Guidance on trophic level specific intakes is provided in the Methodology on Page 4-27.

Bioaccumulation Factors

$$\text{BAF} = \frac{\text{Concentration in Tissue}}{\text{Concentration in Water}}$$

- A BAF reflects for uptake from all media exposures (water, food, sediment).
- A BCF reflects uptake from water only; and can substantially underestimate accumulation for highly hydrophobic chemicals.

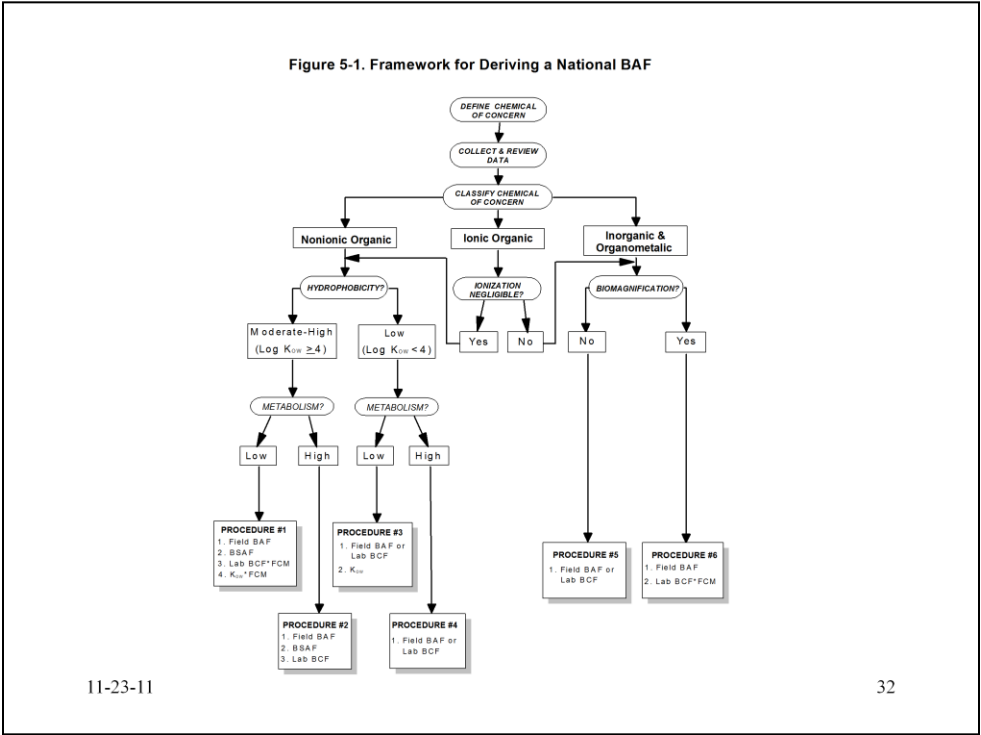
11-23-11

31

Slide 31

U.S. EPA defines the term **bioaccumulation** as the uptake and retention of a chemical by an aquatic organism from all surrounding media (e.g., water, food, sediment) and the term **bioconcentration** as the uptake and retention of a chemical by an aquatic organism from water only.

For some chemicals (particularly those that are highly persistent and hydrophobic (i.e. practically insoluble in water), the magnitude of bioaccumulation by aquatic organisms can be substantially greater than the magnitude of bioconcentration. Thus, an assessment of bioconcentration alone would underestimate the extent of accumulation in aquatic biota for these chemicals. Accordingly, EPA's methodology emphasizes the measurement of chemical **bioaccumulation** by aquatic organisms rather than bioconcentration as was done for the earlier version of the Methodology.



Slide 32.

National BAFs are intended to account for some major chemical, biological, and ecological attributes that can affect bioaccumulation in bodies of water across the United States. The framework for developing a National BAF for different classes of chemicals (i.e., nonionic organic, ionic organic, inorganic and organometallic) is depicted on this slide. Each of the three main branches to the framework applies to a different class of compounds. Different procedures are provided for deriving national BAFs depending on the type of chemical.

For a given type of chemical, one or more BAF derivation **methods** may be used to derive a national BAFs.

Methods for Deriving BAFs

- Field-measured BAF (preferred for all chemicals)
- BAF from a Biota-Sediment Accumulation Factor (BSAF)
- BAF from a laboratory BCF*
- BAF from chemical's Octanol-Water Partition Coefficient (K_{ow})*

* with or without a Food Chain Multiplier (FCM) depending on biomagnification potential

11-23-11

33

Slide 33

The definitions for the parameters that can be used for the PAF are provided below.

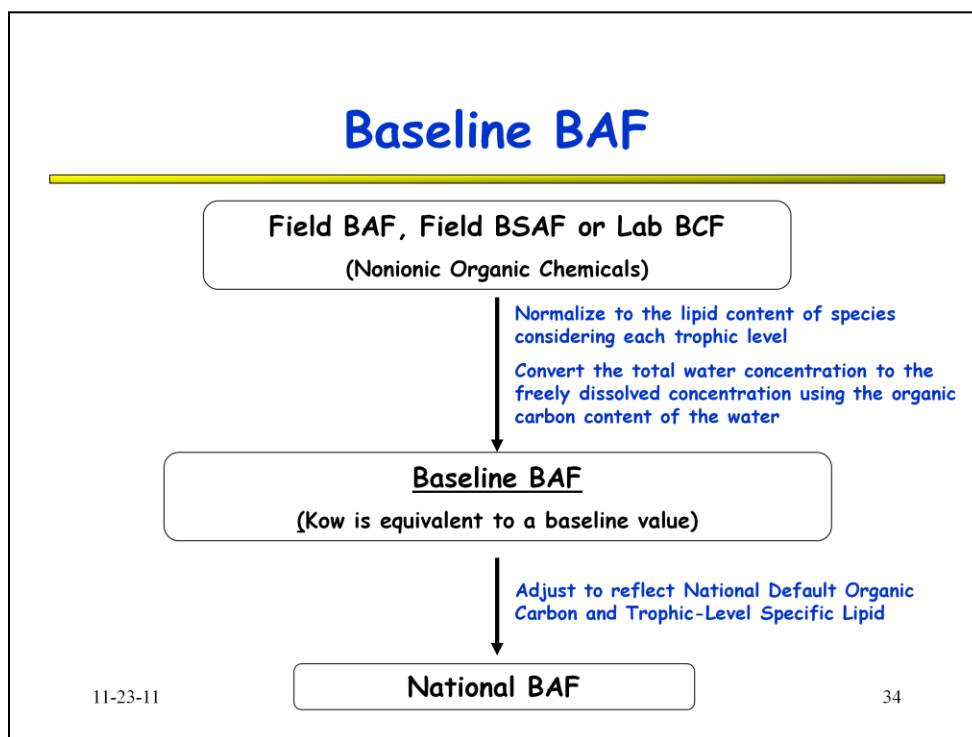
BAF: A field-measured BAF is the most direct measure of bioaccumulation and is the only method that can be used to derive a national BAF for all types of chemicals (i.e., nonionic organic, ionic organic, and inorganic and organometallic chemicals). A field-measured BAF is determined from a field study using measured chemical concentrations in the aquatic organism and its surrounding water. Because field studies are conducted in natural aquatic ecosystems, a field-measured BAF reflects an organism's exposure to a chemical through all relevant exposure pathways (i.e., water, sediment, and diet). A field-measured BAF also reflects any metabolism of a chemical that might occur in the aquatic organism or its food web. Therefore, field-measured BAFs are appropriate for all chemicals, regardless of the extent of chemical metabolism in biota.

BAF Field-measured BSAF. For nonionic organic chemicals, a BAF can also be predicted from BSAFs. A BSAF is similar to a field-measured BAF in that the concentration of a chemical in biota is measured in the field and reflects an organism's exposure to all relevant exposure routes. A BSAF also reflects any chemical metabolism that might occur in the aquatic organism or its food web. However, unlike a field-measured BAF which references the biota concentration to the water concentration, a BSAF references the biota concentration to the sediment concentration. **Use of the BSAF procedure is restricted to organic chemicals which are classified as being moderately to highly hydrophobic and is particularly useful for chemicals that are very difficult to measure in water (e.g. dioxins, PCBs)**

Lab-measured BCF: A laboratory-measured BCF can also be used to estimate a BAF for organic and inorganic chemicals. However, unlike a field-measured BAF or a BAF predicted from a field-measured BSAF, a laboratory-measured BCF only reflects the accumulation of chemical through the water exposure route. Laboratory-measured BCFs may therefore under estimate BAFs for chemicals where accumulation from sediment or dietary sources is significant. In these cases, laboratory-measured BCFs can be multiplied by a FCM to reflect accumulation from non-aqueous (i.e., food chain) pathways of exposure. Since a laboratory-measured BCF is determined using the measured concentration of a chemical in an aquatic organism and its surrounding water, a laboratory-measured BCF reflects any metabolism of the chemical that occurs in the organism, but not in the food web.

Kow: A chemical's octanol-water partition coefficient, or K_{ow} , can also be used to predict a BAF for nonionic organic chemicals. This procedure is appropriate only for nonionic organic chemicals (and certain ionic organic chemicals where similar lipid and organic carbon partitioning behavior applies). For chemicals that are substantially metabolized in biota, the K_{ow} is **not** used to predict the BAF. For nonionic organic chemicals where chemical exposure through the food web is important, use of the K_{ow} alone will under predict the BAF. In such cases, the K_{ow} is adjusted with a FCM similar to the BCF procedure above.

Detailed information on developing national bioaccumulation factors is described in the *Methodology for Deriving Ambient Water Quality Criteria for the Protection of Human Health – Technical Support Document Volume 2: Development of National Bioaccumulation Factors* at: <http://www.epa.gov/waterscience/criteria/humanhealth/method/tsdvol2.pdf>.



Slide 34

For Nonionic Organic Chemicals (these are generally the most highly bioaccumulative chemicals), derivation of the National BAF proceeds through calculation of a Baseline BAF.

Calculating an individual baseline BAF involves normalizing the field-measured BAF, BSAF or laboratory-measured BCF which are based on total concentrations in tissue and water by the lipid content of the study organisms and the freely dissolved concentration in the study water. The freely dissolved water concentration is derived from the total water concentration by adjusting for the organic carbon content of the water (dissolved and particulate organic carbon).

Both the lipid content in the organism and the freely dissolved concentration (as influenced by organic carbon in water) have been shown to be important factors that influence the bioaccumulation of nonionic organic chemicals. Therefore, baseline BAFs, which are expressed on the basis of the chemical concentration in the lipid fraction of tissue and freely dissolved in water, are considered more amenable to being applied across different species and bodies of water than are BAFs or BCF expressed on the basis of the total concentrations in the tissue and water. Because bioaccumulation can be strongly influenced by the trophic position of aquatic organisms (through either biomagnification or physiological differences), extrapolation of baseline BAFs should not be performed between species of different trophic levels.

For nonionic organic chemicals, a baseline BAF is converted to a National BAF by adjusting for national default trophic level values for lipid in fish and dissolved and particulate organic carbon in ambient water.

Fish Tissue Criteria

- HH AWQC Criteria can be expressed as a fish tissue concentration by dropping the Drinking Water Intake and BAF terms
 - Useful for pollutants where BAF is highly variable due to site-specific factors (e.g., Methyl mercury)
 - Allows direct measurement of fish tissue for assessment purposes
 - Requires additional implementation procedures for deriving effluent limits

11-23-11

35

Slide 35

There are times when it may be more important to express the AWQC in terms of the concentration in fish tissue rather than as the concentration in the drinking water. This is appropriate when the BAF value tends to be variable because of site specific situations. When using this approach the AWQC equations are modified by removing the Drinking Water intake and BAF terms providing a fish tissue AWGC in units of mg/g fish intake. When a fish tissue criterion is chosen, the concentrations in edible fish tissues are monitored and additional implementation measures have to be established when deriving effluent limits.

Fish Consumption Advisories

- The EPA Fish Consumption Advisory Program uses a methodology that differs from the AWQC program
 - Both programs use the same toxicological benchmarks (i.e., reference dose and risk specific dose)
- Fish tissue advisories are based on a characterization of measured concentrations in fish tissues from a specific waterbody
- Based on measured fish tissue concentrations and toxicity benchmarks, the allowable "fish meals per month" are calculated and communicated to populations at risk
- Additional information available at:
<http://www.epa.gov/waterscience/fish/advice/es.html>

11-23-11

36

Slide 36

The Fish Consumptions Advisories are not developed using the HH AWQC values. The two programs do rely on the same risk data (RfDs and Risk Specific Doses). Information on the Fish advisory program can be accessed at <http://www.epa.gov/waterscience/fish/advice/es.html>.

Fish Consumption Advisories are expressed in term of the number of fish meals per month that that can be consumed for fish caught in the water body of interest. Measured concentrations of contaminants in fish tissues and the toxicity benchmark determine the number of meals allowed.

Question #1

Which of the following is not a typical element of an assessment for deriving Section 304(a) criteria?

- a. exposure
- b. treatment technologies
- c. bioaccumulation
- d. toxicity
- e. criterion formulation

11-23-11

37

Question #1

Which of the following is not a typical element of an assessment for deriving Section 304(a) criteria?

- a. exposure
- b. treatment technologies
- c. bioaccumulation
- d. toxicity
- e. criterion formulation

b. The other four elements are usually part of an assessment for developing or revising Section 304(a) criteria. Consideration of treatment technologies is not part of the criteria derivation process. Section 304(a) criteria are based solely on human health and do not reflect consideration of economic impacts or technological feasibility.

11-23-11

38

Question #2

True or False?

*Section 304(a)(1) criteria are regulatory limits
States are required to adopt.*

11-23-11

39

Question #2

True or False?

Section 304(a)(1) criteria are regulatory limits States are required to adopt.

False. These criteria are not Federal regulations; however, they are sometimes used by the States and Tribes to establish standards. They present scientific data and guidance on the environmental effect of pollutants, which can be useful to derive regulatory requirements.

11-23-11

40

Question #3

True or False?

Health assessments may include data and information on cancer effects, noncancer effects, and organoleptic effects.

11-23-11

41

Question #3

True or False?

Health assessments may include data and information on cancer effects, noncancer effects, and organoleptic effects.

True. The review of health effects data and relevant information may address carcinogenic endpoints, noncancer endpoints, and/or undesirable taste and odor (organoleptic) effects imparted by a chemical to ambient water.

11-23-11

42

Question #4

True or False?

The RfD is a threshold value below which noncarcinogenic toxic effects are unlikely to occur.

11-23-11

43

Question #4

True or False?

The RfD is a threshold value below which noncarcinogenic toxic effects are unlikely to occur.

True. RfD is the reference dose or the daily estimated exposure to a human population that is not likely to cause deleterious effects over a lifetime. The RfD is expressed as milligrams of toxicant per kilogram of human body weight per day (mg/kg/day).

11-23-11

44

Question #5

The Carcinogenic Potency Slope factor is _____:

- a. RL
- b. RfD
- c. BCF
- d. CSF or q1*
- e. BAF

11-23-11

45

Question #5

The Carcinogenic Potency Slope factor is __:

- a. RL
 - b. RfD
 - c. BCF
 - d. CSF or q1*
 - e. BAF
- d. CSF or SF is the more recent abbreviation for the cancer slope factor. Older assessments use the q1* designation. The CSF is a number that provides an indication of the potential a chemical has to cause cancer in humans. The number is derived from animal studies or epidemiological data on human exposures and use of a linear extrapolation model. The CSF is expressed in units of (mg/kg/day)⁻¹.*

11-23-11

46

Question #6

The process of uptake and accumulation of a chemical through the food chain and water is called?

- a. Food Chain Multiplier
- b. Bioaccumulation
- c. Bioconcentration
- d. RfD
- e. RSC

11-23-11

47

Question #6

The process of uptake and accumulation of a chemical through the food chain and water is called?

- a. Food Chain Multiplier
- b. Bioaccumulation
- c. Bioconcentration
- d. RfD
- e. RSC

b. Bioaccumulation. Bioconcentration considers only uptake of a contaminant through exposure to water

11-23-11

48

Question #7

Which of the following is a method of accounting for multiple sources of exposure when developing human health criteria?

- a. RfD
- b. RfC
- c. RSC
- d. RSD
- e. BAF

11-23-11

49

Question #7

Which of the following is a method of accounting for multiple sources of exposure when developing human health criteria?

- a. RfD
 - b. RfC
 - c. RSC
 - d. RSD
 - e. BAF
- c. RSC. The Relative Source Contribution (RSC) method of considering other exposures (e.g. non-fish dietary intakes, air, soil) determines the RSC factor used in the criteria calculations, which ensures that each criterion is protective of all likely or anticipated exposure, sources/routes relevant to the chemical.*

11-23-11

50

Question #8

An electronic online data base of the U.S. EPA accepted source for RfD values is _____ .

- a. BAF*
- b. BCF*
- c. RfD*
- d. IRIS*
- e. CSF*

11-23-11

51

Question #8

An electronic online data base of the U.S. EPA accepted source for RfD values is ____ .

- a. BAF*
 - b. BCF*
 - c. RfD*
 - d. IRIS*
 - e. CSF*
- d. The Integrated Risk Information System (IRIS) is an electronic online data base of the U.S. EPA that provides chemical-specific risk information on the relationship between chemical exposure and estimated human health effects.*

11-23-11

52

Question #9

True or False?

Section 304(a) criteria are always expressed as chemical concentrations in the water column (e.g., as a mg/L value).

11-23-11

53

Question #9

True or False?

Section 304(a) criteria are always expressed as chemical concentrations in the water column (e.g., as a mg/L value).

False. Although most current Section 304(a) criteria are expressed as water column values, the criteria may also be expressed as fish tissue concentrations (e.g., the methyl mercury criterion). The fish tissue values are very useful when bioaccumulation is highly variable and they allow for direct measurement when assessing compliance monitoring.

11-23-11

54